Applicant: Michael Butters et al. Attorney's Docket No.: 06275-514US1/101315-1P US

Serial No.: 10/581,143
Filed: February 14, 2007
Page: 2 of 15

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application;

Listing of Claims:

(Currently amended) A method for the preparation of a compound of formula (I) or a
pharmaceutically acceptable salt or solvate thereof:

$$O = \bigvee_{N=1}^{NR^2R^3} \bigvee_{S=R^1}$$

in which

 R^1 represents a $C_3\text{-}C_7$ carbocyclic, $C_1\text{-}C_8$ alkyl, $C_2\text{-}C_6$ alkenyl or $C_2\text{-}C_6$ alkynyl group, each of the groups being optionally substituted by one or more substituent groups independently selected from halogen atoms, $-OR^4$, $-NR^5R^6$, $-CONR^5R^6$, $-COOR^7$, $-NR^8COR^9$, $-SR^{10}$, $-SO_2R^{10}$, $-SO_2NR^5R^6$, $-NR^8SO_2R^9$ or a phenyl group, a naphthyl group, or a 5- or 6-membered heteroaryl group containing one or more heteroatoms selected from N, S, and O, wherein the phenyl group, the naphthyl group, and the 5- or 6-membered heteroaryl group are each an aryl or heteroaryl group, both of which may be optionally substituted by one or more substituents independently selected from halogen atoms, cyano, nitro, $-OR^4$, $-NR^5R^6$, $-CONR^5R^6$, $-COOR^7$, $-NR^8COR^9$, $-SR^{10}$, $-SO_2NR^{5}R^6$, $-NR^8SO_2R^9$, C_1 -C6 alkyl or trifluoromethyl groups;

Applicant: Michael Butters et al. Serial No.: 10/581,143 Filed: February 14, 2007 Page: 3 of 15

 R^2 and R^3 each independently represent a hydrogen atom, or a C_3 - C_7 carbocyclic, C_1 - C_8 alkyl, C_2 - C_6 alkenyl or C_2 - C_6 alkynyl group, the latter four groups may be optionally substituted by one or more substituent groups independently selected from:

- (a) halogen atoms, -OR⁴, -NR⁵R⁶, -CONR⁵R⁶, -COOR⁷, -NR⁸COR⁹, -SR¹⁰, -SO₂R¹⁰,
 -SO₂NR⁵R⁶, -NR⁸SO₂R⁹;
- (b) a 3-8 membered ring optionally containing one or more atoms selected from O, S, NR^8 and itself optionally substituted by C_1 - C_3 -alkyl or halogen; or
- (c) a phenyl group, a naphthyl group, or a 5- or 6-membered heteroaryl group containing one or more heteroatoms selected from N, S, and O, wherein the phenyl group, the naphthyl group, and the 5- or 6-membered heteroaryl group are each an aryl group or heteroaryl group each of which may be optionally substituted by one or more substituents independently selected from halogen atoms, cyano, nitro, $-OR^4$, $-NR^5R^6$, $-CONR^5R^6$, $-NR^8COR^9$, $-SO_2NR^3R^6$, $-NR^8SO_2R^9$, C_1-C_6 alkyl and trifluoromethyl groups;

 R^4 represents hydrogen, C_1 - C_6 alkyl or a phenyl group the latter two of which may be optionally substituted by one or more substituent groups independently selected from halogen atoms, phenyl, -OR¹¹ and -NR¹²R¹³

 R^5 and R^6 independently represent a hydrogen atom or a $C_1 \cdot C_6$ alkyl or phenyl group the latter two of which may be optionally substituted by one or more substituent groups independently selected from halogen atoms, phenyl, -OR 14 and -NR $^{15}R^{16}$, -CONR $^{15}R^{16}$, -NR $^{15}COR^{16}$, -SONR $^{15}R^{16}$, NR $^{15}SO_2R^{16}$

or

R⁵ and R⁶ together with the nitrogen atom to which they are attached form a 4- to 7-membered saturated heterocyclic ring system optionally containing a further heteroatom selected from oxygen and nitrogen atoms, which ring system may be optionally substituted by one or more substituent groups independently selected from phenyl, -OR¹⁴, -COOR¹⁴, -NR¹⁵R¹⁶, -CONR¹⁵R¹⁶, -NR¹⁵COR¹⁶, -SONR¹⁵R¹⁶, NR¹⁵SO₂R¹⁶ or C₁-C₆ alkyl, itself optionally substituted by one or more substituents independently selected from halogen atoms and – NR¹⁵R¹⁶ and -OR¹⁷ groups:

Applicant: Michael Butters et al. Serial No.: 10/581,143 Filed: February 14, 2007 Page: 4 of 15

 R^{10} represents a hydrogen atom or a C_{1} – C_{6} -alkyl or a phenyl group, the latter two of which may be optionally substituted by one or more substituent groups independently selected from halogen atoms, phenyl, –OR¹⁷ and –NR¹⁵R¹⁶; and

each of R^7 , R^8 , R^9 , R^{11} , R^{12} , R^{13} , R^{14} R^{15} , R^{16} , R^{17} independently represents a hydrogen atom or a C_1 - C_6 alkyl, or a phenyl group;

which method comprises contacting

$$0 = \bigvee_{N=1}^{L} \bigvee_{N=1}^{N} S - R^{1}$$

wherein L is a leaving group

with a thiazole nitrogen protecting group reagent under appropriate reaction conditions to form a compound of the formula

wherein PG is a protecting group, reacting the compound of formula III with an amine of formula HNR²R³

Applicant: Michael Butters et al. Serial No.: 10/581,143 Filed: February 14, 2007

Page : 5 of 15

to form a compound of formula

$$O = \bigvee_{\substack{N \\ N \\ PG}}^{NR^2R^3} S - R^1$$

and deprotection of the compound of formula II to give a compound of the formula I, and simultaneous or sequential conversion to a pharmaceutically acceptable salt thereof.

- (Original) A method as claimed in claim 1 and wherein R¹ represents an optionally substituted benzyl group.
- 3. (Previously presented) A method as claimed in claim 1 and wherein one of R^2 or R^3 is hydrogen and the other is C_1 - C_8 alkyl substituted by hydroxy and one or more methyl or ethyl groups.
- (Currently Amended) A method as claimed in claim 1 for the preparation of <u>a compound</u> empounds of the formula Ia

Applicant: Michael Butters et al. Serial No.: 10/581,143 Filed: February 14, 2007 Page: 6 of 15

wherein each R^X is independently selected from hydrogen, a C_{1-4} alkyl group optionally substituted by hydroxy, amino, $-O-C_{1-4}$ alkyl, $-S-C_{1-4}$ alkyl, $-N-C_{1-4}$ alkyl, $-N-HSO_2R$, or $-CONR_2$ and provided that both R^X are not hydrogen or amino.

- 5. (Currently Amended) A method as claimed in claim $\underline{4}$ + wherein each R^X is independently selected from hydrogen and hydroxymethyl, provided that both R^X are not hydrogen.
- 6. (Currently Amended) A compound of the formula

$$O = \bigvee_{\substack{N \\ PG}}^{NR^2R^3} \bigvee_{S-R^1}$$

or a pharmaceutically acceptable salt thereof and

 R^1 represents a $C_3\text{-}C_7$ carbocyclic, $C_1\text{-}C_8$ alkyl, $C_2\text{-}C_6$ alkenyl or $C_2\text{-}C_6$ alkynyl group, each of the groups being optionally substituted by one or more substituent groups independently selected from halogen atoms, $\text{-}OR^4$, $\text{-}NR^5R^6$, $\text{-}CONR^5R^6$, $\text{-}COOR^7$, $\text{-}NR^8COR^9$, $\text{-}SR^{10}$, $\text{-}SO_2R^{10}$, $\text{-}SO_2NR^5R^6$, $\text{-}NR^8SO_3R^9$ or a phenyl group, a naphthyl group, or a 5- or 6-membered heteroaryl group containing one or more heteroatoms selected from N, S, and O, wherein the phenyl group, the naphthyl group, and the 5- or 6-membered heteroaryl group are each an aryl or heteroaryl group, both of which may be optionally substituted by one or more substituents independently selected from halogen atoms, cyano, nitro, $\text{-}OR^4$, $\text{-}NR^5R^6$, $\text{-}CONR^5R^6$, $\text{-}COOR^7$, $\text{-}NR^8COR^9$, $\text{-}SR^{10}$, $\text{-}SO_2RR^{5}$ 6, $\text{-}NR^8SO_2R^9$, $\text{C}_1\text{-}C_6$ alkyl or trifluoromethyl groups;

Applicant: Michael Butters et al. Serial No.: 10/581,143 Filed: February 14, 2007 Page: 7 of 15

 R^2 and R^3 each independently represent a hydrogen atom, or a C_3 - C_7 carbocyclic, C_1 - C_8 alkyl, C_2 - C_6 alkenyl or C_2 - C_6 alkynyl group, the latter four groups may be optionally substituted by one or more substituent groups independently selected from:

- (a) halogen atoms, -OR⁴, -NR⁵R⁶, -CONR⁵R⁶, -COOR⁷, -NR⁸COR⁹, -SR¹⁰, -SO₂R¹⁰,
 -SO₂NR⁵R⁶, -NR⁸SO₂R⁹:
- (b) a 3-8 membered ring optionally containing one or more atoms selected from O, S, NR^8 and itself optionally substituted by C_1 - C_3 -alkyl or halogen; or
- (c) a phenyl group, a naphthyl group, or a 5- or 6-membered heteroaryl group containing one or more heteroatoms selected from N, S, and O, wherein the phenyl group, the naphthyl group, and the 5- or 6-membered heteroaryl group are each an aryl group or heteroaryl group each of which may be optionally substituted by one or more substituents independently selected from halogen atoms, cyano, nitro, $-OR^4$, $-NR^5R^6$, $-CONR^5R^6$, $-NR^8COR^9$, $-SO_2NR^3R^6$, $-NR^8SO_2R^9$, C_1-C_6 alkyl and trifluoromethyl groups;

 R^4 represents hydrogen, C_1 - C_6 alkyl or a phenyl group the latter two of which may be optionally substituted by one or more substituent groups independently selected from halogen atoms, phenyl, -OR¹¹ and -NR¹²R¹³

 R^5 and R^6 independently represent a hydrogen atom or a $C_1 \cdot C_6$ alkyl or phenyl group the latter two of which may be optionally substituted by one or more substituent groups independently selected from halogen atoms, phenyl, -OR 14 and -NR $^{15}R^{16}$, -CONR $^{15}R^{16}$, -NR $^{15}COR^{16}$, -SONR $^{15}R^{16}$, NR $^{15}SO_2R^{16}$

or

R⁵ and R⁶ together with the nitrogen atom to which they are attached form a 4- to 7-membered saturated heterocyclic ring system optionally containing a further heteroatom selected from oxygen and nitrogen atoms, which ring system may be optionally substituted by one or more substituent groups independently selected from phenyl, -OR¹⁴, -COOR¹⁴, -NR¹⁵R¹⁶, -CONR¹⁵R¹⁶, -NR¹⁵COR¹⁶, -SONR¹⁵R¹⁶, NR¹⁵SO₂R¹⁶ or C₁-C₆ alkyl, itself optionally substituted by one or more substituents independently selected from halogen atoms and – NR¹⁵R¹⁶ and -OR¹⁷ groups:

Applicant: Michael Butters et al. Serial No.: 10/581,143 Filed: February 14, 2007 Page: 8 of 15

R¹⁰ represents a hydrogen atom or a C₁-C₆-alkyl or a phenyl group, the latter two of which may be optionally substituted by one or more substituent groups independently selected from halogen atoms, phenyl, -OR¹⁷ and -NR¹⁵R¹⁶:

each of R^7 , R^8 , R^9 , R^{11} , R^{12} , R^{13} , R^{14} R^{15} , R^{16} , R^{17} independently represents a hydrogen atom or a C_1 - C_6 alkyl, or a phenyl group; and

PG is a protecting group.

(Currently Amended) A compound of the formula

$$O = \bigvee_{N=1}^{L} \bigvee_{S=R^{1}} S = R^{1}$$

or a pharmaceutically acceptable salt thereof and wherein

 R^1 represents a $C_3\text{-}C_7$ carbocyclic, $C_1\text{-}C_8$ alkyl, $C_2\text{-}C_6$ alkenyl or $C_2\text{-}C_6$ alkynyl group, each of the groups being optionally substituted by one or more substituent groups independently selected from halogen atoms, $\text{-}OR^4$, $\text{-}NR^5R^6$, $\text{-}CONR^5R^6$, $\text{-}COOR^7$, $\text{-}NR^8COR^9$, $\text{-}SR^{10}$, $\text{-}SO_2R^{10}$, $\text{-}SO_2NR^5R^6$, $\text{-}NR^8SO_3R^9$ or a phenyl group, a naphthyl group, or a 5- or 6-membered heteroaryl group containing one or more heteroatoms selected from N, S, and O, wherein the phenyl group, the naphthyl group, and the 5- or 6-membered heteroaryl group are each or-an aryl-or-heteroaryl group, both of which may be optionally substituted by one or more substituents independently selected from halogen atoms, cyano, nitro, $\text{-}OR^4$, $\text{-}NR^5R^6$, $\text{-}CONR^5R^6$, $\text{-}COOR^7$, $\text{-}NR^8COR^9$, $\text{-}SR^{10}$, $\text{-}SO_2RR^{10}$, $\text{-}SO_2NR^5R^6$, $\text{-}NR^8SO_2R^9$, $\text{C}_1\text{-}C_6$ alkyl or trifluoromethyl groups;

Applicant: Michael Butters et al. Attorney's Docket No.: 06275-514US1/101315-1P US

Serial No.: 10/581,143 Filed: February 14, 2007 Page: 9 of 15

 R^4 represents hydrogen, C_1 - C_6 alkyl or a phenyl group the latter two of which may be optionally substituted by one or more substituent groups independently selected from halogen atoms, phenyl, -OR¹¹ and -NR¹²R¹³

 R^5 and R^6 independently represent a hydrogen atom or a C_1 - C_6 alkyl or phenyl group the latter two of which may be optionally substituted by one or more substituent groups independently selected from halogen atoms, phenyl, -OR¹⁴ and -NR¹⁵R¹⁶, -CONR¹⁵R¹⁶, -NR¹⁵COR¹⁶, -SONR¹⁵R¹⁶, NR¹⁵SO₂R¹⁶

or

R⁵ and R⁶ together with the nitrogen atom to which they are attached form a 4- to 7-membered saturated heterocyclic ring system optionally containing a further heteroatom selected from oxygen and nitrogen atoms, which ring system may be optionally substituted by one or more substituent groups independently selected from phenyl, -OR¹⁴, -COOR¹⁴, -NR¹⁵R¹⁶, -CONR¹⁵R¹⁶, -NR¹⁵COR¹⁶, -SONR¹⁵R¹⁶, NR¹⁵SO₂R¹⁶ or C₁-C₆ alkyl, itself optionally substituted by one or more substituents independently selected from halogen atoms and – NR¹⁵R¹⁶ and -OR¹⁷ groups;

 R^{10} represents a hydrogen atom or a C_1 - C_6 -alkyl or a phenyl group, the latter two of which may be optionally substituted by one or more substituent groups independently selected from halogen atoms, phenyl, $-OR^{17}$ and $-NR^{15}R^{16}$;

each of R^7 , R^8 , R^9 , R^{11} , R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , R^{17} independently represents a hydrogen atom or a C_1 - C_6 alkyl, or a phenyl group;

L is a leaving group; and

PG is a protecting group.

8. (Currently Amended) A compound of the formula

Applicant: Michael Butters et al. Serial No.: 10/581,143 Filed: February 14, 2007 Page: 10 of 15

or a pharmaceutically acceptable salt thereof and wherein

 R^1 represents a C_3 - C_7 carbocyclic, C_1 - C_8 alkyl, C_2 - C_6 alkenyl or C_2 - C_6 alkynyl group, each of the groups being optionally substituted by one or more substituent groups independently selected from halogen atoms, $-OR^4$, $-NR^5R^6$, $-CONR^5R^6$, $-COOR^7$, $-NR^8COR^9$, $-SR^{10}$, $-SO_2R^{10}$, $-SO_2R^{10}$, $-SO_2R^{5}R^6$, $-NR^8SO_3R^9$ or a phenyl group, a naphthyl group, or a 5- or 6-membered heteroaryl group containing one or more heteroatoms selected from N, S, and O, wherein the phenyl group, the naphthyl group, and the 5- or 6-membered heteroaryl group are each or an aryl or heteroaryl group, both of which may be optionally substituted by one or more substituents independently selected from halogen atoms, cyano, nitro, $-OR^4$, $-NR^5R^6$, $-CONR^5R^6$, $-COOR^7$, $-NR^8COR^9$, $-SR^{10}$, $-SO_2R^{10}$, $-SO_2NR^5R^6$, $-NR^8SO_2R^9$, C_1-C_6 alkyl or trifluoromethyl groups; R^4 represents hydrogen, C_1-C_6 alkyl or a phenyl group the latter two of which may be optionally substituted by one or more substituent groups independently selected from halogen atoms, phenyl, $-OR^{11}$ and $-NR^{12}R^{13}$

 R^5 and R^6 independently represent a hydrogen atom or a $C_1 \cdot C_6$ alkyl or phenyl group the latter two of which may be optionally substituted by one or more substituent groups independently selected from halogen atoms, phenyl, $-OR^{14}$ and $-NR^{15}R^{16}$, $-CONR^{15}R^{16}$, $-NR^{15}COR^{16}$, $-SONR^{15}R^{16}$, $NR^{15}SO_2R^{16}$

or

R⁵ and R⁶ together with the nitrogen atom to which they are attached form a 4- to 7-membered saturated heterocyclic ring system optionally containing a further heteroatom selected from oxygen and nitrogen atoms, which ring system may be optionally substituted by one or more substituent groups independently selected from phenyl, -OR¹⁴, -COOR¹⁴, -NR¹⁵R¹⁶,

Applicant: Michael Butters et al. Serial No.: 10/581,143 Filed: February 14, 2007 Page: 11 of 15

-CONR¹⁵R¹⁶, -NR¹⁵COR¹⁶, -SONR¹⁵R¹⁶, NR¹⁵SO₂R¹⁶ or C₁-C₆ alkyl, itself optionally substituted by one or more substituents independently selected from halogen atoms and – NR¹⁵R¹⁶ and -OR¹⁷ grouns:

 R^{10} represents a hydrogen atom or a C_1 - C_6 -alkyl or a phenyl group, the latter two of which may be optionally substituted by one or more substituent groups independently selected from halogen atoms, phenyl, $-OR^{17}$ and $-NR^{15}R^{16}$:

each of R^7 , R^8 , R^9 , R^{11} , R^{12} , R^{13} , R^{14} R^{15} , R^{16} , R^{17} independently represents a hydrogen atom or a C_1 - C_6 alkyl, or a phenyl group; and

L is a leaving group other than chlorine.

9. (Currently Amended) A compound of the formula

or a pharmaceutically acceptable salt thereof and wherein

 R^1 represents a $C_3\text{-}C_7$ carbocyclic, $C_1\text{-}C_8$ alkyl, $C_2\text{-}C_6$ alkenyl or $C_2\text{-}C_6$ alkynyl group, each of the groups being optionally substituted by one or more substituent groups independently selected from halogen atoms, $-OR^4$, $-NR^5R^6$, $-CONR^5R^6$, $-COOR^7$, $-NR^8COR^9$, $-SR^{10}$, $-SO_2R^{10}$, $-SO_2NR^5R^6$, $-NR^8SO_2R^9$ or a phenyl group, a naphthyl group, or a 5- or 6-membered heteroaryl group containing one or more heteroatoms selected from N, S, and O, wherein the phenyl group, the naphthyl group, and the 5- or 6-membered heteroaryl group are each an aryl or heteroaryl group, both of which may be optionally substituted by one or more substituents independently selected from halogen atoms, cyano, nitro, $-OR^4$, $-NR^5R^6$, $-CONR^5R^6$, $-COOR^7$, $-NR^8COR^9$, $-SR^{10}$, $-SO_2NR^5R^6$, $-NR^8SO_2R^9$, C_1-C_6 alkyl or trifluoromethyl groups;

Applicant: Michael Butters et al. Attorney's Docket No.: 06275-514US1 / 101315-1P US

Serial No.: 10/581,143
Filed: February 14, 2007
Page: 12 of 15

 R^4 represents hydrogen, C_1 - C_6 alkyl or a phenyl group the latter two of which may be optionally substituted by one or more substituent groups independently selected from halogen atoms, phenyl, -OR¹¹ and -NR¹²R¹³

 R^5 and R^6 independently represent a hydrogen atom or a C_1 - C_6 alkyl or phenyl group the latter two of which may be optionally substituted by one or more substituent groups independently selected from halogen atoms, phenyl, -OR¹⁴ and -NR¹⁵R¹⁶, -CONR¹⁵R¹⁶, -NR¹⁵COR¹⁶, -SONR¹⁵R¹⁶, NR¹⁵SO₂R¹⁶

or

R⁵ and R⁶ together with the nitrogen atom to which they are attached form a 4- to 7-membered saturated heterocyclic ring system optionally containing a further heteroatom selected from oxygen and nitrogen atoms, which ring system may be optionally substituted by one or more substituent groups independently selected from phenyl, -OR¹⁴, -COOR¹⁴, -NR¹⁵R¹⁶, -CONR¹⁵R¹⁶, -NR¹⁵COR¹⁶, -SONR¹⁵R¹⁶, NR¹⁵SO₂R¹⁶ or C₁-C₆ alkyl, itself optionally substituted by one or more substituents independently selected from halogen atoms and – NR¹⁵R¹⁶ and -OR¹⁷ groups;

 R^{10} represents a hydrogen atom or a $C_1\text{-}C_6\text{-}alkyl$ or a phenyl group, the latter two of which may be optionally substituted by one or more substituent groups independently selected from halogen atoms, phenyl, -OR 17 and -NR $^{15}R^{16}$; and

each of R^7 , R^8 , R^9 , R^{11} , R^{12} , R^{13} , R^{14} R^{15} , R^{16} , R^{17} independently represents a hydrogen atom or a C_1 - C_6 alkyl, or a phenyl group.

10. (Cancelled)